REMARKS

I. Sequence Compliance

Applicants have amended the specification to make reference to SEQ ID NOS and have added an additional sequence to the sequence listing. The sequence listing as amended does not contain new matter as it simply includes the sequence designated in Figure 2 as "HepI" as SEQ ID NO:6.

II. Specification

The Examiner has noted that the numbering of claims was not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. Applicants apologize for the error and have renumbered the claims.

The Applicants have inserted reference to SEQ ID NOS: where appropriate.

III. Rejection of the Claims under 35 USC § 112—Enablement

The Examiner has rejected claims 23, 26-33, 34, and 46-47 as being nonenabled as to some of the polypeptide fragments recited in the claims.

The Examiner states:

> [The specification] does not reasonably provide enablement for use of polypeptides or compositions comprising amino acids 42 through 129 or 42 through 161 or 130 through 534 or 162 through 534 of SEQ ID NO:2.

And that this is so because:

> The specification does not support the broad scope of the claims which encompass the use of specific polypeptide fragments of SEQ IUD NO:2 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting ***heparanase activity;*** (B) the general tolerance of heparanase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying amino acid residues in SEQ ID NO:2 with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.
> Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including fragments of SEQ ID NO:2 without showing that such fragments have ***activity***.

The Applicants respectfully submit that the Examiner's rejection does not comply with the law to the extent that it requires that the disclosed fragments must have enzymatic activity to be patentable. On the contrary, the law merely requires that the fragments have a patentable utility and that the specification provide guidance on how to make and use the invention without undue experimentation.

The specification at pages 8 and 9 and Figure 1 and Example 2 at page 38, notes that applicant's fragments are the result of intracellular processing of full length SEQ ID NO:2. The fragments themselves therefore have utility as size markers to establish that processing of the full length protein has occurred. The fragments may be used directly as size markers for such purposes but also may be used for the generation of antibodies directed against them (with or without other sequences attached) to access intracellular processing. That this is so in the haparanase art is well known and graphically demonstrated by *Levy-Adams et al*, Biochemical and Biophysical Research Communications 308: 885-891 (2003) (Exhibit 1) and by *Fairbanks et al.* J Biol Chem 274: (42): 29587-90 (1999) (Exhibit 2).

III. Rejection of the Claims under 35 USC § 112—Written Description

The Examiner states that

> [T]he claims are directed to a genus of polypeptides that have not been described in the claims. No description has been provided of all the polypeptide sequences encompassed by the applicants which would indicate that they had possession of the claimed genus of polypeptides. .... The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus.

The Examiner therefore apparently takes the position that any claim which recites the transitional term "comprising" lacks written description because it includes within its scope unrecited elements. If the Examiner continues to hold this view Applicants would request that authority to support that position be made of record in this case.

Further, the Patent Office's most recent guidelines, require analysis of claims for relevant identifying characteristics sufficient to show that the Applicant was in possession of the claimed

genus. In the instant case the relevant identifying structural characteristic is SEQ ID NO: 2. This is the sequence that defines the genus, and one skilled in the art can evaluate any polypeptide to determine whether a fragment is one recited in the claims[1]. The Patent Office has identified no other structural characteristics that are necessary to identify the genus. In such circumstances, the rejection should be withdrawn.

Appropriate analogy can be drawn to examples in the Patent Office's "training materials." Example 14 of the written description guideline training materials relate to a claim to a protein genus defined by a 95% identity limitation with the disclosure of a single species. The Patent Office concludes that the single sequence disclosed is representative of the genus, and concludes that the claim meets the requirements of § 112, first paragraph. Analogously, the sequence taught in SEQ ID NO: 2 of the present application is representative of the of what is presently being claimed.

Claim 33 (renumbered) of the present application also recites " an epitope." Because epitopes are antigenic determinants, appropriate analogy also can be drawn to Example 16 of the training materials, which relate to antibodies. The Patent Office acknowledges that the level of skill and knowledge in the art of antibodies was "high and advanced" and that antibody production was a "mature technology." The Patent Office acknowledges "the routine art-recognized method of making antibodies to fully characterized antigens," and concludes that a claim direct to *any* antibody to an antigen meets the written description requirements. It should be readily apparent that this logic should likewise extend to any epitope of the completely characterized antigen sequence.

The Examples in the training materials that find lack of written description relate to examples that are factually distinct from the present claims. For example, such examples relate to examples that have "essential" or "critical" elements that are allegedly not described. no such elements have been identified in the present rejection.

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[1] The Applicants arguments are not intended as an admission that the Patent Office's current guidelines represent a proper characterization of the law or the way that courts construe § 112, first paragraph.

The Examiner alleges that the specification does not adequately describe the scope of the claimed subject matter. The rejection contains general statements about "different functions " and conserved regions that would be critical for those features. If the Examiner maintains this rejection, the Applicants request clarification of what "function" is deemed critical for written description of the claimed fragments. The fragments of Heparanase II which are specifically pointed out in the claims and SEQ ID NO:2 itself are useful for accessing cellular processing of heparanase II.

IV. Claim Rejections ---35 USC § 112-Second Paragraph

The Examiner states:

> In response to the previous Office action, applicants have amended the claims by deleting reference to "human heparanase-II". This mainly appears to be due to the confusion with respect to the 35 U.S.C. 112, 2nd paragraph rejection for the recitation of "heparanase-II". In response to that rejection all that applicants had to do was reiterate that the difference between the known heparanase in the prior art and the instant heparanase is in the amino acid sequence information. However, applicants have deleted all references to the term which described the activity of the polypeptide Those skilled in the art would not how to use the claimed polypeptide fragments without knowing what activity the polypeptides have. Hence the above rejection is maintained

Applicants would remind the Examiner that the previous office action in which he stated:

> Claims 23-33 are drawn to an enzyme labeled heparanase II. It is not clear to the Examiner as to how one skilled in the art will be able to distinguish "heparanase II" from other human heparanase already disclosed in the prior art. A perusal of the specification does not provide a specific or distinguishing assay based on which the instant enzyme can be identified as "heparanase II" The only information provided is that the amino acid sequence ***that is different from that already disclosed in the prior art*** (figure 2). Therefore it is not clear to the Examiner as to whether the instant is a simple variant of the already known heparanase or an entirely different class of heparanase and as to how those skilled in the art can identify the above protein without first analyzing its amino acid sequence. (emphasis added)

Because it is clear that the Examiner was most certainly aware that SEQ ID NO:2 differed from the prior art, Applicants eliminated the recitation of "heparanase II" from the

claims because it would appear to be the only possible or conceivable source of the Examiner's confusion. The Examiner now appears amazingly to be requiring that Applicants amend the claim further to again recite "heparanase II" because

> "applicants have deleted all references to the term which described the activity of the polypeptide Those skilled in the art would not how to use the claimed polypeptide fragments without knowing what activity the polypeptides have."

Once again, the Applicants would like to point out to the Examiner that the claims clearly and distinctly claim their invention with or without the recitation of "heparanase II" Applicants would further point the Examiner to *In re Tanksley*, 37 USPQ 2d 1382, 1386 (B.P.A.I. 1994)

> In our judgment, a patent applicant is entitled to a reasonable degree of latitude in complying with the second paragraph of 35 U.S.C. § 112 and the examiner may not dictate the literal terms of the claims . . . Stated another way, a patent applicant must comply with 35 U.S.C. § 112, second paragraph, but just how the applicant does so, within reason, is within applicant's discretion.

Applicants would request that they be afforded the degree of latitude in claiming their invention that *Tanksley* requires.

Lastly, to the extent the Examiner is taking the position that the claims must "describe the activity of the polypeptide" or "how to use" the polypeptide, Applicants would respectfully remind the Examiner that the specification more than adequately describes the functions and uses of the of the polypeptide. If the Examiner is aware of any authority which supports his position that claims must teach "how to use", Applicants respectfully request that such authority be made of record or that the rejection be withdrawn.

To facilitate prosecution Applicants have amended claims 30-32 to recite a functional limitation and to recite the transitional term"consisting essentially of".

VIII. Claim Rejections—35 USC § 102

Claims 23-29 29-31, 33, 45-46 were rejected as allegedly being anticipated by Freeman et al. (1998). With the Examiner stating:

> However, Examiner takes the position that the amino acid sequence of an enzyme (a

> polypeptide) is an inherent characteristic and therefore as the enzyme in the reference has the same activity as described by the applicants, the enzyme in the reference and the enzyme claimed by the applicants are one and the same.

Applicants would respectfully remind the examiner of the standard set forth in *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 20 USPQ 2d 1746, 1749 (Fed. Cir. 1991)

> To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter **is necessarily present in the thing described** in the reference and that it would be so recognized by persons of ordinary skill. *In re Oelrich*, 212 USPQ 323, 326 (C.C.P.A. 1981) (quoting *Hansgirg v. Kemmer*, 40 USPQ 665, 667 (C.C.P.A. 1939)) provides:Inherency, however may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. (Emphasis added)

And

Ex parte Levy, 17 USPQ 2d 1461, 1464 (B.P.A.I. 1990)

> [T]he examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art.

The Examiner has not met the burder required by *Continental Can* and *Levy*. He provides no basis in fact or technical reasoning other than simply stating that he "takes the position" that *Freeman* anticipates Applicant's invention. *Freeman* simply discloses heparanase activity and a molecular weight.

Applicant's specification specifically makes reference to prior teaching of "heparanase I" and shows that the sequences of heparanse I and heparanase II are different sequences. The Examiner provides absolutely no reasoning or showing of fact which would establish that *Freeman* ***necessarily*** discloses heparanase II rather than heparanase I or some other human heparanase as is required by *Continental Can* and *Levy*. Applicants would therefore respectfully request that this rejection be withdrawn.

Claims 21-23, 26-27 and 33 were rejected under 35 USC 102(e) as being anticipated by Fiscella et al. WO 01/79253 with an apparent effective date of April 18, 2000. Applicants have submitted a Rule 1.132 declaration executed by Ms. Julie Lyons to overcome the reference. The Examiner contends that a Rule 1.132 declaration is "improper" for overcoming the above

rejection and has maintained the prior rejection.

Rule 1.131 states the following:

> When any claim of an application or a pat ent under reexamination is rejected under 35 U.S.C. 102(a) or (e), or 35 U.S.C. 103 based on a U.S. patent to another or others which is prior art under 35 U.S.C. 102(a) or (e) and which substantially shows or describes but does not claim the same patentable invention, as defined in 1.601(n), or on reference to a foreign patent or to a printed publication, **the inventor of the subject matter of the rejected claim, the owner of the patent under reexamination, or the party qualified under §§1.42, 1.43, or 1.47, may submit an appropriate oath or declaration to overcome the patent or publication**. The oath or declaration must include facts showing a completion of the invention in this country or in a NAFTA or WTO member country before the filing date of the application on which the U.S. patent issued, or before the date of the foreign patent, or before the date of the printed publication. When an appropriate oath or declaration is made, the patent or publication cited shall not bar the grant of a patent to the inventor or the confirmation of the patentability of the claims of the patent, unless the date of such patent or printed publication is more than one year prior to the date on which the inventor's or patent owner's application was filed in this country. (Emphasis added)

Rule 1.132 states the following:

> When any claim of an application or a patent under reexamination is rejected or objected to,any evidence submitted to traverse the rejection or objection **on a basis not otherwise provided for** must be by way of an oath or declaration under this section.
> (Emphasis added)

Ms. Lyons is not an inventor, or owner of the patent, or a party qualified under §§1.42, 1.43, or 1.47 and as such cannot properly execute a Rule 1.131 declaration. Ms. Lyons however, does have knowledge that establishes that date of Applicant's invention and therefore can supply a declaration establishing the date certain documents were received into her office. Her statement therefore provides evidence "on a basis not otherwise provided for" as described in Rule 1.132.

If the Examiner is aware of authority contrary to a plain reading of the rules which states that a Rule 1.131 declaration is the **only** evidence that may be received to

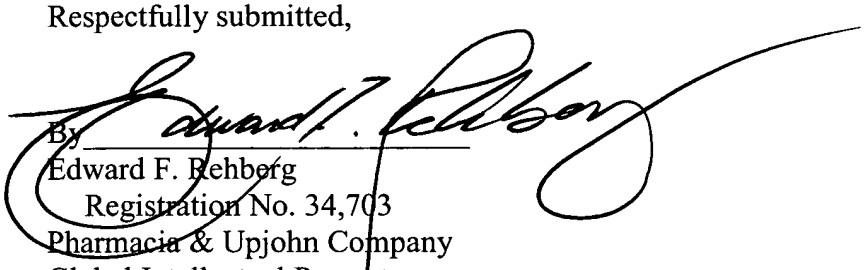
establish invention prior to the date of a reference, Applicants respectfully request that the authority be made of record. In the alternative the Applicants respectfully request that the rejection based on *Fiscella* be withdrawn.

IX. Conclusion

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to issue.

Dated: April 6, 2003

Respectfully submitted,



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